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ORIGINAL ARTICLE

Role of QuantiFERON-TB-Gold In Tube assay for active and latent tuberculosis infection in investigation of tuberculosis outbreak in a university

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Background: Identification and monitoring of active tuberculosis (TB) and latent tuberculosis infection (LTBI) are the key steps to prevent transmission during a TB outbreak. The aim of this study was to evaluate the role of QuantiFERON-TB-Gold In Tube assay (QFT-GIT) in the investigation of active TB and LTBI cases during a TB outbreak in a university.
Methods: In this study, enrolled students and teachers were evaluated with chest radiograph, questionnaire, and QFT-GIT test. The diagnosis of active pulmonary TB was based on sputum studies and chest radiographs. The questionnaire, which covered demographic information, underlying diseases, and environmental exposures, was applied to assess the association of risk factors by multiple logistic regressions.

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Results: A total of 159 participants completed the study protocol. Positive QFT-GIT results were demonstrated in class A (75.7%; 25/33), class B (57.1%; 20/35), and class C (37.5%; 3/8) in institute 1; class D (17.3%; 8/46) in institute 2; and class E (3.1%; 1/32) in institute 3; but none among the (0/5) administrative officers, who comprised the control group. "Number of contact with active TB cases" was strongly associated and correlated with the prediction of a positive QFT-GIT result in multivariate analysis (odds ratio = 1.99; 95% confidence interval, 1.52—2.61; $p < 0.0001$). Seven cases progressed to active TB infection, all showing positive QFT-GIT results (100%; 7/7).
Conclusion: Inclusion of QFT-GIT may be helpful in controlling and monitoring of active TB and LTBI cases during an investigation of a TB outbreak. The finding demonstrated that the QFT-GIT test was useful in accurately identifying infected and uninfected students, permitting rapid intervention.

Introduction

Identification and monitoring of active tuberculosis (TB) infection and latent TB infection (LTBI) are the important steps of infection control to stop transmission during a TB outbreak, especially in a school setting where students live and study in crowded, enclosed spaces. Large-scale TB outbreaks have occurred in schools around the world.[1—4] Diagnosis of active pulmonary TB was based on clinical examination, chest radiography, acid-fast stain, a molecular method, and sputum culture.[5] Identification of LTBI was suggested by methods of tuberculin skin test (TST) and interferon-gamma (IFN-γ) around the world including Taiwan.[6] Until recently, TST was the available tool for the diagnosis of LTBI; however, it had major drawbacks, which included the possibility of obtaining false-positive results because of cross-reactivity with nontuberculous mycobacteria or with the bacillus Calmette—Guerin (BCG) vaccination that had been used in Taiwan and many countries.[5] QuantiFERON-TB Gold In Tube assay (QFT-GIT; Cellestis Limited, Carnegie, Victoria, Australia) was an immunologic assay that measured the IFN-γ released by T lymphocytes sensitized with the *Mycobacterium tuberculosis*-specific antigens ESAT-6 and CFP-10. The comparable sensitivity but higher specificity of this assay (in comparison with TST) had been known to aid in the diagnosis of both active TB infection and LTBI.[7,8]

Although a higher incidence of TB infection was reported in Taiwan, the prevalence of LTBI in the community was uncertain.[9] Our study was designed to assess the active TB infection and LTBI burden in BCG-vaccinated students using QFT-GIT and to determine the environmental and lifestyle factors that predisposed certain individuals to the infection. This study demonstrated the role of the QFT-GIT assay in detecting TB infection, including active cases and LTBI, during a TB outbreak in a university in Taiwan.

Materials and methods

Study populations

In November 2010, a 22-year-old female student suffered from fever and cough, and her chest radiograph was compatible with a primary TB complex infection. *M. tuberculosis* was isolated from the sputum culture. The following year, two of her classmates were confirmed to have active pulmonary TB infection. An immediate contact investigation (chest radiograph, questionnaires, QFT-GIT) was performed for all of the index case's classmates and for the other students in different institutes sharing the same classroom in this university. Closer contact was defined as exposure of 8 hours per day, or more than 40 hours in the same environment with transmissible active TB cases according to the definition of the Centers for Disease Control (CDC) in Taiwan.[6] Students who had close contact with the index case for 8 months were screened for TB infection and LTBI. The university environment was assessed with ventilation evaluation. To prioritize students for TB screening, the study was conducted among the students to identify the factors associated with close contact with the index case as per the criteria of the CDC in Taiwan.[5] The index patient was interviewed about her personal, social, and class activities during the school deployment. A questionnaire was designed to collect information on potential exposure factors among the study participants. All personnel had been evaluated using the questionnaire and blood examination of QFT-GIT. Individuals with positive QFT-GIT results were referred to hospitals. History taking, physical examination, acid-fast stain, culture, and polymerase chain reaction (PCR) for tuberculosis were evaluated if an abnormal finding of chest radiography was noted. Individuals with negative QFT-GIT results were followed up. The flow diagram for this study is shown in Fig. 1. We examined all participants who had positive QFT-GIT results with chest radiograph (CXR) during the 1st year. We checked for the presence of TB infection using sputum acid-fast bacilli (AFB) culture, and PCR in patients whose CXR indicated infiltration and who had a cough. The CXR, AFB, and PCR for sputum were interpreted by other investigators. The investigators who read the final CXR and took the patients' history to determine the patient's TB status were blinded to the QFT-GIT results.

AFB microscopy and culture

For acid-fast staining, decontaminated sputum was fixed onto a slide, and the number of AFB per field for an average